UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

08/13/2012

MEMORANDUM:

Subject: EPA Reg. No.: 62719-42/ Reldan F Insecticidal Chemical
DP Barcode: 403821/403822/403823/403825/403826
Case No.: N/A

From: Boris Yurchak, Chemist
Risk Management and Implementation Branch V (7508P)
Pesticide Re-evaluation Division

To: Joel Wolf, CRM
Risk Management and Implementation Branch III (7508P)
Pesticide Re-evaluation Division

Applicant: Dow AgroSciences LLC,
9330 Zionsville Road
Indianapolis, IN 46268

FORMULATION FROM EPA Reg. No. 62719-42 LABEL:

Active Ingredient(s):	% by wt.
Chlorpyrifos-methyl [0,0-dimethyl 0-(3,5,6-trichloro-2-pyridyl) phosphorothioate]:	97%
Other Ingredient(s):	3%
Total	100.0%

BACKGROUND: In response to the registration review DCI for Chlorpyrifos-methyl [0,0-dimethyl 0-(3,5,6-trichloro-2-pyridyl) phosphorothioate] (059102), the registrant is submitting five acute toxicity studies to support their product EPA Reg. No. 62719-42. The MRID's are as follows: 488681-01 (870.1100), 488681-02 (870.1200), 488681-03 (870.1300), 488681-04 (870.2400), 488681-05 (870.2500), 449069-01 & 449890-01 (870.2600). The test material used in each of the studies is the subject product.

RECOMMENDATIONS:

- The acute toxicity studies (81-1, 81-2, 81-3, 81-4, 81-5) submitted are acceptable to support the reregistration of EPA Reg. No. **62719-42**.
- The Skin Sensitization Study (81-6) is unacceptable due to the lack of a positive control study. A new study should be cited or submitted.

The acute toxicity profile for EPA Reg. No. **62719-42** is currently:

Acute Oral	III	Acceptable (LD_{50}>%2,000 mg/kg)
Acute Dermal	IV	Acceptable (LD_{50}>5,000 mg/kg)
Acute Inhalation	IV	Acceptable (LC_{50}>2.48 mg/L)
Primary Eye	IV	Acceptable
Primary Skin	IV	Acceptable
Skin Sensitization	---------	Unacceptable

DATA REVIEW FOR ACUTE ORAL TOXICITY (§81-1, 870.1100)

Product Manager: Venus Eagle, 1
MRID No.: 488681-01

Reviewer: Boris Yurchak
Study Completion Date: 05/23/2012
Report No.: 120084

Testing Facility: JAI Research Foundation, Valvada- 396 108, Gujarat, India
Author: R. Verma

Quality Assurance (40 CFR §160.12): Included

Test Material: Chlorpyrifos Methyl TGAI, White Crystalline Solid
Species: Wistar female rat
Age: 10 – 11 weeks
Weight: 203 – 218 g
Source: Animal Breeding facility, JAI Research Foundation

Method used for calculation of LD_{50}: Acute Toxic Class Method

Conclusion:

1. **LD_{50} (mg/kg):** > 2,000 mg/kg (based on EPA classification)

2. **Toxicity Category:** III **Classification**: Acceptable

Procedure (Deviations from §81-1): none

Results: Limit Test

Set No.	Animal No.	Dose level, (mg/kg)	Short-term Outcome (0-6 h)	Long-term Outcome (1-14 day)
1	1	2,000	S	S
	2	Idem	S	S
	3	Idem	S	S
2	4	Idem	S	S
	5	Idem	S	S
	6	Idem	S	S

S- Survival, D- Death

Observations: All animals gained weight and appeared normal during the time period of the study.

Gross Necropsy: No observable abnormalities were noted.

DATA REVIEW FOR ACUTE DERMAL TOXICITY (§81-2, 870.1200)

Product Manager: Venus Eagle, 1
MRID No.: 488681-02

Reviewer: Boris Yurchak
Study Completion Date: 05/16/2012
Report No.: 120085

Testing Facility: JAI Research Foundation, Valvada- 396 108, Gujarat, India
Author: R. Verma

Quality Assurance (40 CFR §160.12): Included

Test Material: Chlorpyrifos Methyl TGAI, White Crystalline Solid
Species: Wistar 5 males and 5 female rats
Age: 9 – 11 weeks
Weight: 203 – 218 g
Source: Animal Breeding facility, JAI Research Foundation

Method used for calculation of LD_{50}: Probit analysis method

Summary:

1. **LD_{50} (mg/kg):** >5,000 mg/kg

2. **Toxicity Category:** IV **Classification:** Acceptable

Procedure (Deviations From §81-2): none

Results: **Reported Mortality**

Dosage (mg/kg)	(number deaths/number tested)		
	Males	Females	Combined
5000	0/5	0/5	0/10

Preparation/Application:

Twenty four hours prior to application of the test material, the dorsal area and the trunk were clipped free of hair. The test substance was placed on a porous gauze dressing (not more than 8 ply) and applied to the 4 cm x 5 cm intact dose site (approximately 10 % of the body surface) on each animal. The test item was held in contact with the skin using a non-irritating tape (Medi tape 330 hypo-allergenic surgical tape). At the end of the exposure period (24 h), the residual test item was removed using cotton soaked in distilled water.

Observations: All animals showed no appreciable change in body weight and appeared normal during the time period of the study.

Gross Necropsy Findings: No any abnormalities were noted.

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (§81-3, 870.1300)

Product Manager: Venus Eagle, 1
MRID No.: 488681-03

Reviewer: Boris Yurchak
Study Completion Date: 05/11/2012
Report No.: 121027

Testing Facility: Toxicology & Environmental Research and Consulting, the Dow Chemical Company, Midland, Michigan 48674
Authors: S.M. Krieger, M.S. and C.R. Garlinghouse, B.S.

Quality Assurance (40 CFR §160.12): Included

Test Material: Chlorpyrifos Methyl, aerosol
Species: F344/DuCrl 5 males and 5 female rats
Age: 7 – 8 weeks
Weight, g: 167-184 (m), 127-134 (f)
Source: Charles River (Kingston, New York)

Summary:

1. **LC_{50} (mg/L):** > 2.48 mg/L
2. **MMAD** (µm): 2.32 **GSD** (µm): 2.24
3. **Tox. Category:** IV **Classification:** Acceptable

Procedure (Deviation From §81-3): none

Results:

Reported Mortality

Exposure Concentration (mg/L)	(number deaths/number tested)		
	Males	Females	combined
2.48	0/5	0/5	0/10

Chamber Atmosphere		
Dose Level, mg/L	MMAD, µm	GSD, µm
2.48	2.32	2.24
2.48	2.79	2.44
2.48	1.98	1.86

Chamber Environment	Dose Level, mg/L
	2.48
Chamber volume, cm^3	42400
Airflow, Lpm	26
Nominal concentration, mg/L	29.2
Temperature (°C)	21.7±0.5
Relative Humidity %	9.9±6.4

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (§81-4, 870.2400)

Product Manager: Venus Eagle, 1
MRID No.: 488681-04

Reviewer: Boris Yurchak
Study Completion Date: 05/16/2012
Report No.: 120087

Testing Facility: JAI Research Foundation, Valvada- 396 108, Gujarat, India
Author: R. Verma

Quality Assurance (40 CFR §160.12): Included

Test Material: Chlorpyrifos Methyl TGAI, White Crystalline Solid
Species: three New Zealand White female rabbits (*oryctolagus cuniculus*)
Age: 16-17 weeks
Weight: 2.340 – 2.618 kg
Source: Animal Breeding facility, JAI Research Foundation
Dosage: One-tenth of milliliter (0.1 mL) of the test substance

Summary:

Toxicity Category: IV **Classification:** Acceptable

Procedure (Deviations From §81-4): none

Results:

Observations	(number "positive"/number tested)			
	Hours			
	1	24	48	72
Corneal Opacity	0/3	0/3	0/3	0/3
Iris	0/3	0/3	0/3	0/3
Conjunctivae				
Redness	0/3	0/3	0/3	0/3
Chemosis	0/3	0/3	0/3	0/3

There was no corneal opacity or iritis observed in any treated eye during the study.

DATA REVIEW FOR DERMAL IRRITATION TESTING (§81-5, 870.2500)

Product Manager: Venus Eagle, 1
MRID No.: 488681-05

Reviewer: Boris Yurchak
Study Completion Date: 05/16/2012
Report No.: 120086

Testing Facility: JAI Research Foundation, Valvada- 396 108, Gujarat, India
Author: R. Verma

Quality Assurance (40 CFR §160.12): Included

Test Material: Chlorpyrifos Methyl TGAI, White Crystalline Solid
Species: three New Zealand White male rabbits (*oryctolagus cuniculus*)
Age: 16-17 weeks
Weight: 2.562 – 2.609 kg
Source: Animal Breeding facility, JAI Research Foundation
Dosage: 500 mg of the test substance for 4 hours following application to 10% of body surface area

Summary:

1. **Toxicity Category:** IV

2. **Classification:** Acceptable PDII ≈ 0.7

Procedure (Deviations From §81-5): none

Application: A quantity of 500 mg chloropyrifos methyl TGAI moistened with 0.5 mL distilled water was applied evenly to one of the clipped sites of each rabbit and on the clipped site, 0.5 mL distilled water was applied. The latter served as the control site. The treated and the control sites were covered with gauze patches of approximately 6 cm^2 (gauze rolled) which was not more than 8-ply and was secured at the margins by non-irritating tape (Medi tape 330 hypo-allergic surgical tape) to prevent evaporation of the test item and to ensure that the rabbits did not ingest it. At the end of the 4 h exposure period 9day 00, the residual test item was removed with cotton soaked in distilled water.

Results:

Observations after patch Removal	(number "positive"/number tested)			
	Hours			
	1	24	48	72
Erythema	3/3	3/3	2/3	0/3
Oedema	0/3	0/3	0/3	0/3

Very slight Erythema was evident at 1 and 24 h in all the three rabbits and resolved by 48 h in one rabbit while in case of 2 rabbits it resolved by 72 h.

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (§81-6, 870.2600)

Product Manager: Venus Eagle, 1
MRID Nos.: 449069-01, 449890-01

Reviewer: Boris Yurchak
Study Completion Date: 05/20/1985; 12/01/1999
Report No.: DET 474; RFB 120199

Testing Facility: Hazleton Laboratories Europe (Covance Laboratories) Ltd, UK
Author: J.R. Jones, R.F. Bischoff

Quality Assurance (40 CFR §160.12): Not Included

Test Material: Chlorpyrifos Methyl TGAI, White Crystalline Solid
Species: 28 Hartley albino guinea pig (14 male, 14 female)
Age: young adult
Weight: 275-712 g
Source: Hacking and Churchill, Huntingdon

Positive Control Material: not given/not applied

Method: Buehler

Summary:

1. Skin Sensitization of the subject product has not been determined properly
2. **Classification:** Not Acceptable

Procedure (Deviation From §81-6): Information on the positive control study, including the positive control substance used, the method used, and the time conducted is not presented in the MRIDs provided and, therefore, does not meet requirements of the OPPTS 870.2600.

Procedure:

A lint pad (2.5 cm x 2.5 cm) wetted with test article (0.3 mL), at a concentration of 100% w/v, was applied to the left flank of each guinea pig for a contact period of 6 h. The lint pads were held in place with an overlapping impermeable occlusive tape and secured by elastic adhesive bandage wound round the torso of the animal. The treatment was repeated 7 and 14 days after the initial exposure on the same site, which was shaved the day before each application.

Two weeks after the induction phase (day 29), the test animals of group I were challenged by application of test article at a concentration of 100% w/v in polyethylene glycol on a closed patch on the right flank of each animal. An identical patch was placed on the opposite flank treated with vehicle alone. After 6 hours the patches were removed. The following day all animals were treated with depilatory cream on the challenge sites, rinsed thoroughly and dried with a disposable towel.

Untreated control animals of group II each received an identical application of the test solution or vehicle on day 29 using the same procedure as for the treatment group I.

Three hours after depilation the challenge sites from both groups were evaluated (24 hour reading). The evaluation was repeated 24 hours later (48 hour reading).

Results:

Slight patchy redness was noted in all test sites exposed to 100% w/v Reldan F and in 2 test sites exposed to a concentration of 50% w/v. A concentration of 100% w/v was used for the main study. No adverse skin reactions were noted on exposure to test article or vehicle alone on test and control animals. These results indicated that Reldan F does not cause delayed contact hypersensitivity in the guinea pig using the Buehler test.
Nevertheless, the results cannot be accepted since the positive control test was not performed (see MRID No. 449890-01).